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REACTIONS OF 2-IMINOTHIAZOLIDINE DERIVATIVES WITH ACRYLONITRILE, METHYL ACRYLATE, AND METHYL IODIDE

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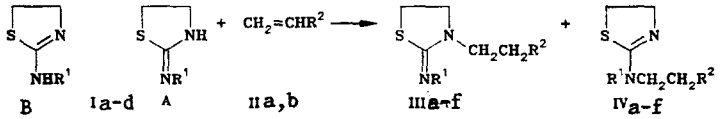
UDC 547.789.1:541.621

In all cases the cyanoethylation, carbomethoxyethylation, and methylation of 2-amino(imino)thiazoli(di)ne derivatives that are substituted at the exocyclic nitrogen atom lead to the simultaneous formation of isomeric products with 2-iminothiazolidine and 2-amino-Δ^2-thiazoline structures.

The question as to the form (A or B) in which 2-iminothioazolidine derivatives exist remains open to discussion [1, 2]. The phosphorylation and thiophosphorylation of substances of the A or B type, which lead to the initial formation of a product of reaction at the ring nitrogen atom, which under certain conditions exists in equilibrium with the product of substitution at the exocyclic nitrogen atom, were described in [3]. The interconversions were explained by their ability to undergo phosphorotropic isomerization [3].

It seemed of interest to study transformations of this type in which possibilities of this sort would be excluded. For this we studied the reaction of 2-allyliminothiazolidine (Ia) with acrylonitrile in benzene and acetonitrile.

It was established that a mixture of two substances IIIa and IVa (with similar properties) that is characterized by two spots on the chromatogram and two C=N absorption bands in the IR spectra (Table 1) is formed from chromatographically pure Ia, which has one absorption band of the C=N bond in its IR spectrum [2]. To confirm this we realized the alternative synthesis of IIIa by the method in [4]. According to the IR spectral data, III: IVa is ~2:1 and depends only slightly on the nature of the solvent.



I a $R^1=CH_2CH=CH_2$; b $R^1=C_6H_5$; c $R^1=C_2H_5$; d $R^1=CH_2C_6H_5$; II a $R^2=CN$; b $R^2=COOCH_3$; III, IV a $R^1=CH_2CH=CH_2$, $R^2=CN$; b $R^1=C_6H_5$, $R^2=CN$; c $R^1=C_2H_5$, $R^2=CN$; d $R^1=CH_2C_6H_5$, $R^2=CN$; e $R^1=CH_2CH=CH_2$, $R^2=COOCH_3$; f $R^1=C_6H_5$, $R^2=COOCH_3$

Institute of Biophysics, Ministry of Public Health of the USSR, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 563-566, April, 1990. Original article submitted July 13, 1988; revision submitted June 20, 1989.

 0009-3122/90/2604-0482$12.50

TABLE 1. Reaction Conditions and Characteristics of the III and IV Formed

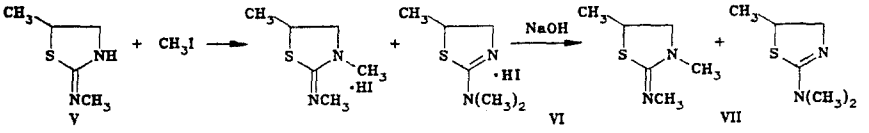
Reacting components (solvent)	R_f (system)		IR spectrum, C=N, cm^{-1}	III:IV, %
	III	IV		
Ia+IIa (benzene, acetonitrile)	0,55 (1)	0,38 (1)	1640, 1608	65:35
Ib + IIa (benzene, acetonitrile)	0,62 (1)	0,42 (1)	1630, 1615 sh.	—*
Ic + IIa (benzene)	0,45 (2)	0,32 (2)	1643, 1610	75:25
Id + IIa (benzene)	0,46 (3)	0,22 (3)	1641, 1610	75:25
Ia + IIb (benzene, acetonitrile)	0,62 (1)	0,34 (1)	1637, 1610**	65:35
Ib + IIb (benzene, acetonitrile)	0,56 (1)	0,20 (1)	1633***	Only III
V + CH_3I (benzene, acetone)	0,43 (3)	0,60 (3)	1650, 1615	70:30
Ib + CH_3I (benzene, acetone)	0,79 (4)	0,46 (4)	1635i , 1616	10:90

*The band is poorly resolved, and quantitative evaluation was hindered.
**Compounds IIIe and IVe could not be synthesized by an alternative method; the C=N frequency of IIIa was used for comparison.
***Compounds IIIf and IVf could not be synthesized by an alternative method; the C=N frequency of IIIb was used for comparison.

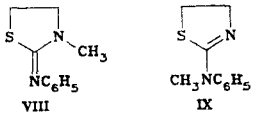
The reaction of acrylonitrile with 2-phenyliminothiazolidine (Ib), 2-ethyliminothiazolidine (Ic), and 2-benzyliminothiazolidine (Id) proceeds similarly with the formation of IIIb-d–IVb-d pairs. The assignment of the spots on the chromatograms and the frequencies of the absorption bands in the IR spectra was accomplished by means of model compounds IIIc, d, which were obtained by the method in [4], and IIIb [5]; the formation of primarily the iminothiazolidine structure was observed in each of the investigated examples (Table 1).

The addition of thiazolidine Ia to methyl acrylate also depends only slightly on the nature of the solvent and leads to the formation of IIIe and IVe. An interesting peculiarity is observed in the reaction of Ib with methyl acrylate both in benzene and in acetonitrile. According to TLC data, the formation of two substances with R_f 0.45 and 0.86 occurs initially; the spot with R_f 0.86 is predominant and becomes the only spot upon completion of the reaction, and the IR spectrum of the mixture contains only one C=N absorption band, which corresponds to imino form III (Table 1). This makes it possible to assume that the addition of Ib to methyl acrylate is reversible, as a result of which the initially formed IVf undergoes complete conversion to thiazolidine IIIf. This sort of pattern is observed when the reaction is carried out in both benzene and acetonitrile.

According to the TLC and IR spectral data, two substances are also formed in the alkylation of 2-methylimino-5-methylthiazolidine (V) with methyl iodide. The assignment of them by means of the R_f values and the C=N absorption bands was made in comparison with the model compound 2-dimethylamino-5-methyl-Δ^2-thiazoline (VII) [1]; primarily 2-methylimino-3,5-dimethylthiazolidine (VI) was formed in the reaction under consideration.



The reaction of methyl iodide with Ib with heating and at room temperature leads to a mixture of isomers VIII and IX, the assignment of which was made by means of model compound VIII [6].



It is interesting that, in contrast to all of the reactions described above, the formation of thiazoline isomer IX predominates in this reaction.

Model compounds IIIa-d were synthesized by an alternative method from N-substituted N'-(2-hydroxyethyl)-N'-(2-cyanoethyl)thiocarbamides Xa-d obtained from the corresponding isothiocyantes and N-(2-hydroxyethyl)-2-aminopropionitrile (XI).

X a R=$CH_2CH=CH_2$; b R=C_6H_5; c R=C_2H_5; d R=$CH_2C_6H_5$

The side formation of thiazolidine Ia was observed in the alternative synthesis of IIIa. This indicates the ability of IIIa to undergo thermal dissociation with splitting out of acrylonitrile, which does not undergo readdition but forms resinous products. To avoid this the operations in the alternative synthesis of IIIa-d should be carried out at no higher than 150°C.

EXPERIMENTAL

The IR spectra of solutions of the compounds in CCl_4 in 0.1-mm KBr cuvettes were recorded with a Perkin–Elmer 398 spectrometer. The following systems were used for chromatography: activity II aluminum oxide, mobile phases ether–CH_2Cl_2 (2:3) (system 1), ether–CH_2Cl_2 (3:7) (system 2), ether–chloroform (2:3) (system 3), ether (system 4); Silufol UV-254, mobile phases butanol–acetic acid–water (4:1:5) (system 5), ammonia–chloroform–2-propanol (1:8:4) (system 6), ethanol (system 7); the chromatograms were developed with iodine vapors.

Satisfactory results of elementary analysis for the C, H, N, and S content were obtained for all of the new compounds.

Reaction of Ia with Acrylonitrile. A) A solution of 3.6 g (25 mmole) of Ia and 2.0 g (38 mmole) of acrylonitrile in 35 ml of benzene was heated at 70°C until the spot of starting Ia (system 1) vanished. The solvent was then removed, and the residue was fractionated in vacuo to give 3.1 g (63%) of a substance with bp 63-66°C (3 Pa), d_4^{20} 1.1233, n_D^{20} 1.5473, and MR_D 55.08. Calculated MR_D (for IIIa): 55.72. $C_9H_{13}N_3S$.

B) A solution of 0.5 g (3.5 mmole) of Ia and 0.3 g (5.3 mmole) of acrylonitrile in 15 ml of acetonitrile was heated at 70°C until the spot of starting Ia vanished. Data on the substances obtained by methods A and B are presented in Table 1.

The cyanoethylation of Ib in benzene and acetonitrile and of Ic, d in benzene and the carbethoxymethylation of Ia, b in benzene and acetonitrile were carried out by method B (Table 1).

2-Allylamino-3-(2-cyanoethyl)thiazolidine (IIIa, $C_9H_{13}N_3S$). A 2.7 g (27 mmole) sample of allyl isothiocyanate was added dropwise to a solution of 3.1 g (27 mmole) of XI in 40 ml of methylene chloride, and the mixture was refluxed for 30 min. The solvent was removed to give Xa with R_f 0.78, 0.73, and 0.85 (systems 5, 6, and 7, respectively). A mixture of 5.8 g (27 mmole) of Xa and 2.2 g (9 mmole) of phosphorus acid hexaethyltriamide was stirred for 15 min at 150°C with removal of the liberated diethylamine by distillation. The mixture was then cooled, 10 ml of concentrated HCl was added dropwise, and the solution was washed with ether. A 15-ml sample of 50% KOH solution was added dropwise, 20 ml of water was added, and the mixture was extracted with ether. The ether extract was dried with $MgSO_4$, the ether was removed, and the residue was fractionated in vacuo to give 2.4 g (46%) of thiazolidine IIIa with bp 74-77°C (3 Pa), d_4^{20} 1.1192, n_D^{20} 1.5478, and MR_D 55.32 (calculated value 55.72).

2-Ethylimino-3-(2-cyanoethyl)thiazolidine (IIIc, $C_8H_{13}N_3S$). A 2.5-g (28.3 mmole) sample of ethyl isothiocyanate was added dropwise with stirring to a solution of 3.2 g (28.3 mmole) of XI in 40 ml of methylene chloride, and the mixture was refluxed for 30 min. The solvent was removed to give Xc with R_f 0.71, 0.84, and 0.75 (systems 5, 6, and 7, respectively). A mixture of 5.7 g (28.3 mmole) of Xc and 7.0 g (28.3 mmole) of phosphorous acid hexaethyltriamide was stirred at 140°C until a heterogeneous mass formed, during which the liberated diethylamine was removed by distillation. The mixture was then cooled, 15 ml of concentrated HCl was added dropwise, 15 ml of water was added, and the mixture was filtered. The solution was washed with ether, 20 ml of 50% KOH solution was added dropwise, the mixture was extracted with ether, and the extract was dried with $MgSO_4$. The ether was removed, and the residue was fractionated in vacuo to give 2.0 g (38%) of IIIc with bp 57-59°C (3 Pa), d_4^{20} 1.1056, n_D^{20} 1.5317, and MR_D 51.27 (calculated value 51.38).

N-Benzyl-N'-(2-hydroxyethyl)-N'-(2-cyanoethyl)thiocarbamide (Xd, $C_{13}H_{17}N_3OS$). A 9.6-g (64.1 mmole) sample of benzyl isothiocyanate was added dropwise with stirring to a solution of 7.3 g (64.1 mmole) of XI in 80 ml of methylene chloride, and the mixture was refluxed for 30 min. The solvent was removed, and the residue was recrystallized from benzene–ethanol (40:1) to give 15.5 g (91%) of thiocarbamate Xd with mp 83-85°C.

2-Benzylimino-3-(2-cyanoethyl)thiazolidine (IIId, $C_{13}H_{15}N_3S$). A mixture of 6.8 g (26 mmole) of thiocarbamate Xd and 6.4 g (26 mmole) of phosphorous acid hexaethyltriamide was stirred at 140°C until a heterogeneous mass formed, during which the liberated diethylamine was removed by distillation. The mixture was then cooled, 15 ml of concentrated HCl was added dropwise, 15 ml of water was added, and the mixture was filtered. A 20-ml sample of 50% KOH solution was added dropwise to the filtrate, and the liberated oil was extracted with ether. The extract was dried with $MgSO_4$, and the ether was removed to give 5.0 g (79%) of thiazolidine IIId with d_4^{20} 1.1393, n_D^{20}, 1.5816, and MR_D 71.73 (calculated value 71.19).

Reaction of V with Methyl Iodide. A solution of 1.0 g (7.7 mmole) of V and 1.6 g (11.5 mmole) of methyl iodide in 20 ml of benzene (acetone) was heated at 60°C until the spot of starting V vanished (system 3). The solvent was then removed, the residue was dissolved in water, 2 ml of 50% KOH solution was added, and the mixture was extracted with ether. The extract was dried with $MgSO_4$, and the ether was removed (Table 1).

Reaction of Ib with Methyl Iodide in Benzene. A solution of 1.0 g (5.6 mmole) of Ib and 1.2 g (8.3 mmole) of methyl iodide in 30 ml of benzene was stirred with refluxing until the spot of starting Ib vanished (system 4). The precipitated crystals were separated and dissolved in water, 2 ml of 50% KOH solution was added, and the mixture was extracted with ether. The extract was dried with $MgSO_4$, and the ether was removed (Table 1).

Reaction of Ib with Methyl Iodide in Acetone. A solution of 0.8 g (4.5 mmole) of Ib and 1.0 g (6.8 mmole) of methyl iodide in 20 ml of acetone was stirred at room temperature until the spot of starting Ib vanished (system 4). The acetone was then removed, the residue was dissolved in water, and the solution was worked up as indicated above (Table 1).

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